

Please replace the paragraph from lines 10-29 on page 40 with:

Individual colonies are selected, cut with AsuII and BamHI, and the size of the

a2 AsuII/BamHI fragment determined. Colonies in which both the primer 1 and primer 2 sequences are correctly inserted are further amplified, and cut with AsuII and BamHI to produce the gene activation construct

cgaaggcaggcagccagcgagggagagcgagcggcgagccggagcgaggaaATCGAAGGTTCGAATCCTTC
CCCCACCACCATCACTTCAAAAGTCCGAAAGAAATCTGCTCCCTGCTTGTGTGG
AGGTGCGTAGTGTGCGAGTAAAATTAAAGCTACAACAAGGCAAGGCTTGACC
GACAATTGCATGAAGAATCTGCTTAGGGTTAGGCCTTGCCTGCTCGCGATGTA
CGGGCCAGATATACGCGTTGACATTGATTATTGACTAGTTATTAAATAGTAATCAATT
ACGGGGTCATTAGTCATAGCCCATAATGGAGTTCCCGCTTACATAACTACGGTA
AATGGCCCGCCTGGCTGACCGCCAACGACCCCCGCCATTGACGTCAATAATGAC
GTATGTTCCCATAGTAACGCCAATAGGGACTTCCATTGACGTCAATGGGTGGACTA
TTTACGGTAAACTGCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCC
CCCTATTGACGTCAATGACGGTAAATGGCCCGCTGGCATTATGCCAGTACATGAC
CTTATGGGACTTCCACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATG
GTGATGCGGTTTGGCAGTACATCAATGGCGTGGATAGCGGTTGACTCACGGGA
TTTCCAAGTCTCCACCCATTGACGTCAATGGAGTTGGCACCAAATCAA
CGGGACTTCCAAAATGTCGTAACAACCTCCGCCATTGACGCAAATGGCGGTAG
GCGTGTACGGTGGAGGTCTATATAAGCAGAGCTCTGGCTAACTAGAGAACCCA
CTGCTTACTGGCTTATCGAAATTAAATACGACTCACTATAGGGAGACCCAAGCTGGT
ACCGAGCTCGGATCgtctggaaagcgcaagagagagcgcacacacccgcgcgcactcg (SEQ ID
No. 25)

Please replace the first paragraph on page 53 with:

In an illustrative embodiment, the *ptc* therapeutic can be an antisense construct for inhibiting the expression of *patched*, e.g., to mimic the inhibition of *patched* by *hedgehog*.

a3 Exemplary antisense constructs include:

5'-GTCCTGGCGCCGCCGCCGTGCC (SEQ ID No. 26)

5'-TTCCGATGACCGGCCTTCGCGGTGA (SEQ ID No. 27)

5'-GTGCACGGAAAGGTGCAGGCCACACT (SEQ ID No. 28)

The replacement paragraphs presented above incorporate changes as indicated by the marked-up versions below.

In an exemplary embodiment, portions of the 5' flanking region of the human Shh gene are amplified using primers which add restriction sites, to generate the following fragments

5'-gcgcgcttcgaaGCGAGGCAGCCAGCGAGGGAGAGAGCGAGCGGGCGAGCCGGAGC-GAGGAAatcgatgcgcgc (primer 1) (SEQ ID No. 23)

5'-gcgcgcagatctGGGAAAGCGCAAGAGAGAGCGCACACGCACACACACCCGCCGCGCG-CACTCGggatccgcgcgc (primer 2) (SEQ ID No. 24)

Individual colonies are selected, cut with AsuII and BamHI, and the size of the AsuII/BamHI fragment determined. Colonies in which both the primer 1 and primer 2 sequences are correctly inserted are further amplified, and cut with AsuII and BamHI to produce the gene activation construct

cgaaggcaggcagccagcgaggagagcgagcggcgagccggagcgaggaaATCGAAGGTTGAATCCTTC
CCCCACCACCATCACTTCAAAAGTCCGAAAGAATCTGCTCCCTGCTTGTGTGTTGG
AGGTCGCTGAGTAGTGCGCGAGTAAAATTAAAGCTACAACAAGGCAAGGCTTGACC
GACAATTGCATGAAGAACATCTGCTTAGGGTTAGGCCTTGCCTGCTTCGCGATGTA
CGGGCCAGATATACCGCTGACATTGATTATTGACTAGTTATTAAATAGTAATCAATT
ACGGGGTCATTAGTTCATAGCCATATGGAGTTCCCGCTTACATAACTACGGTA
AATGGCCCCTGGCTGACGCCAACGACCCCCGCCATTGACGTCAATAATGAC
GTATGTTCCCATAGTAACGCCAATAGGGACTTCCATTGACGTCAATGGGTGGACTA
TTTACGGTAAACTGCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCC
CCCTATTGACGTCAATGACGGTAAATGGCCCGCTGGCATTATGCCAGTACATGAC
CTTATGGGACTTCCACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATG
GTGATGCGGTTTGGCAGTACATCAATGGCGTGGATAGCGGTTGACTCACGGGA
TTCCAAGTCTCCACCCATTGACGTCAATGGAGTTGTTGGCACCAAATCAA
CGGGACTTCCAAAATGTCGTAACAACCTCCGCCCCATTGACGCAAATGGCGGTAG
GCGTGTACGGTGGAGGTCTATATAAGCAGAGCTCTGGCTAACTAGAGAACCCA
CTGCTTACTGGCTTATCGAAATTAAATACGACTCACTATAGGGAGACCCAAGCTGGT
ACCGAGCTCGGATCgatctggaaagcgcaagagagagcgcacacccgcgcgcactcg (SEQ ID
No. 25)